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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/709,577	05/14/2004	Itzhak Bentwich	050992.0202.02USCP	3576

37808 7590 09/20/2007

ROSETTA-GENOMICS
c/o PSWS
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SUITE 1000
KANSAS CITY, MO 64112

EXAMINER
WOLLENBERGER, LOUIS V

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
09/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/709,577	BENTWICH ET AL.	
	Examiner	Art Unit	
	Louis V. Wollenberger	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-31 and 33* is/are pending in the application.

4a) Of the above claim(s) *26,29 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,27,28,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 March 2007 and 14 May 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/5/06; 10/6/06 (2)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions/Status/Amendment/Claims

Applicant's election without traverse of Group I, claims 25-32, drawn to an isolated nucleic acid comprising at least 16 nucleotides of SEQ ID NO:10,068,310, in the reply filed on 7/2/07, is acknowledged. Also acknowledged is Applicant's election without traverse of SEQ ID NO:7,002,375. Applicant states SEQ ID NO: 7,002,375 corresponds to target gene ACTN4, having GenBank Accession No. NM_004924.

With entry of the amendment filed on 7/2/07, claims 25-31 and 33 are pending. Claims 26, 29, and 33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions, there being no allowable generic or linking claim. Election was made without traverse in the reply filed 7/2/07.

Claims 25, 27, 28, 30, and 31 are examined herein.

Sequence Listing

The objection to the sequence listing is withdrawn.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25, 27, 28, 30, and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 is drawn in part to an RNA equivalent of a nucleic acid 16-120 nucleotides in length comprising at least 16 consecutive nucleotides of SEQ ID NO:10,068,310. However, the Office's records show that SEQ ID NO: 10,068,310 is an RNA. Thus, it is unclear what is meant by the limitation an "RNA equivalent" of an RNA. The structures specifically included and/excluded by this limitation are unclear. Accordingly, one of skill in the art would not be apprised of the metes and bounds of the claim as a whole.

Adding to the confusion are instant claims 27 and 28, drawn directly or indirectly to the nucleic acid of claim 25, wherein the nucleic acid comprises SEQ ID NO:7,002,375. However, SEQ ID NO:7,002,375 is a DNA, having the following sequence: acatacacgggaaacctctttt.

Thus, it is unclear how any DNA, much less that defined by the claim, can comprise at least 16 consecutive nucleotides of an RNA. Claims dependent therefrom are rejected therefor.

Correction is required.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25, 27, 28, 30, and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claim 25, submitted on 3/21/07, claims an isolated nucleic acid consisting of 16-120 nucleotides comprising at least 16 nucleotides of SEQ ID NO:10,068,310.

MPEP 2163, Section II, Part A, states in part that there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed, *Wertheim*, 541 F.2d at 262, 191 USPQ at 96; however, with respect to newly added or amended claims, applicant should show support in the original disclosure for the new or amended claims.

In the instant case, Applicant points to Table 10, lines 345905-345934, Table 1, and Table 2, which tables are contained on compact discs submitted with the original application. Applicant describes how individual sequences set forth therein are related to one another, stating, for example, that the sequences set forth in Tables 1 and 2 together make up a precursor sequence referred to as GR5737, which applicant claims represents SEQ ID NO:10,068,310. Table 10 states GR5737 is an RNA precursor sequence that is processed into at least 82 separate RNA precursor sequences. Applicant submits that, altogether, the information set forth in the separate tables establishes possession of not only the 44,000-nucleotide sequence corresponding to SEQ ID NO:10,068,310, but all nucleic acids of 16-120 nts in length identical and complementary to this sequence, as well as RNA equivalents thereof.

However, Applicant's explanation of how the individual sequences may be cobbled together to produce a super sequence cannot supplement or replace the original disclosure. What is needed is explicit, implicit, or inherent description of the claimed nucleic acid sequence itself in the specification as originially filed.

To start, SEQ ID NO:10,068,310 does not appear to be disclosed in the original sequence listing, the basis for which would appear to be mega tables 1-15. A complete sequence listing

was not submitted until 3/21/07, after filing. This sequence listing adds SEQ ID NO:10,068,310, which does not appear in the application as originally filed.

Support is not readily found in either the 245-page specification or in any of the mega tables 1-15 submitted with the application (MPEP 2164.04).

Furthermore, it is unclear how one of skill would clearly recognize SEQ ID NO:10,068,310 from the disclosure cited in Tables 1, 2, and 10. For example, each of the 82 RNA products derived from GR5737 according to Table 10 are not found in tables 1 and 2, and it is unclear how one of skill would recognize the relationship between GR5737 and the sequences set forth in tables 1 and 2 from the original disclosure.

Thus, a review of the specification fails to find clear, antecedent support for SEQ ID NO:10,068,310.

Accordingly, the instant claims as a whole are rejected for lack of written description support.

Claim Rejections - 35 USC § 101 and 112, First Paragraph

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25, 27, 28, 30, and 31 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility, a credible asserted utility, or a well established utility.

The claims are drawn to an isolated nucleic acid sequence consisting of 16 to 120 nucleotides comprising a) at least 16 consecutive nucleotides of SEQ ID NO: 10,068,310; b) an RNA equivalent of (a); c) a sequence at least 80/% identical to (a) or (b); or d) the complement of any one of (a)-(c).

In one embodiment, claims 27 and 30, the sequence is SEQ ID NO:7,002,375, a 22-nucleotide DNA.

Also claimed are vectors thereof.

At the outset, it is noted that the instant application is extremely large, comprising a 245-page specification, and at least 15 different mega tables, disclosing over 10 million different nucleic acid sequences, said to be precursor and processed miRNAs, with homologies to a variety of different targets, and having a wide variety of asserted utilities based on that homology.

SEQ ID NO: 10,068,310 is not found in the application as filed. Further, written description and enabling support describing and teaching methods for using instant SEQ ID NO:7,002,375 for a specific and substantial utility is not readily found therein.

Applicant states in the Remarks filed 7/2/07 that SEQ ID NO:7,002,375 relates to target gene ACTN4 having GenBank Accession No. NM_004924, but does not indicate where such support for may be found in the instant application as originally filed.

The specification teaches that Micro RNAs (miRNAs), are short ~22nt non-coding regulatory RNA oligonucleotides, found in a wide range of species, believed to function as specific gene translation repressors, sometimes involved in cell-differentiation.

The specification teaches a bioinformatic method for detecting putative miRNA-like precursor sequences in the genome of an organism. Further bioinformatics processing is then used to predict the single stranded miRNAs likely produced from such sequences. Finally, the sequences of the predicted miRNAs are compared to sequences of known genes to identify potential targets and possible biological functions of the miRNAs.

While the specification teaches miRNA prediction, support is not readily found showing that the claimed miRNAs are actually produced in any cell or organism, or even if produced artificially, would lead to any biological effect of any immediate, real world value. No biologically relevant data, nor any intrinsic or extrinsic evidence is found in the instant application confirming any of the asserted utilities.

In the instant case the only utility readily identified has to do with that set forth in the Remarks filed 7/2/07, wherein Applicant submits a relationship to ACTN4, also known as actinin-4. However, this disclosure is not found in the application as filed.

The prior art (Honda et al., 1998, *J. Cell Biology* 140:1383-1393) teaches a possible association of actinin-4 with cell motility, which may assist in cancer metastasis. However, the prior art does not teach how to treat cancer or any other disease by direct inhibition of actinin-4 expression, nor any indication that expression of any of the nucleic acids now claimed would inhibit cancer or any other disease associated with actinin-4.

Indeed, the asserted utility and target gene of this and thousands of other miRNA-like sequences appears to be based purely on bioinformatic methods for predicting RNA folding and potential gene targets.

Post-filing art indicates that while prediction software and bioinformatics methods significantly narrow the field of possible sequences, they do not substitute for or render unnecessary the need for biological validation.

Krutzfeldt et al. (2006) *Nature Genetics* 38:514-519 state that, in general, the basis for these types of prediction programs is the degree of sequence complementarity between a miRNA and a target UTR, including the presence of a consecutive string of base pairs at the 5′ end of the miRNA known as a 'seed' or 'nucleus', and the cross-species conservation of this binding site. On average, 200 genes are predicted to be regulated by a single miRNA. The authors further state that reviewing the data provided by these algorithms determining candidate targets uncovers the entire gamut of gene categories, such as transcription factors, protein kinases, vesicular trafficking molecules and membrane receptors, suggesting that there is no apparent bias towards one particular function.

Bentwich (2005) *FEBS Lett.* 5904-5910 teaches that biological validation is necessary to raise the specificity and sensitivity of microRNA prediction algorithms, implying that predictions based on such algorithms need validation and that prediction does not guarantee that such a sequence exists or has the function assigned to it by the software.

Accordingly, while the ability to predict hairpin-like structures and potential gene targets from genomic sequence information appears to be within the state of the art, Krutzfeldt et al. and Bentwich teach that validating the true biological function of any predicted miRNA sequence

requires analyzing miRNA expression patterns, as well as testing the effects of miRNA overexpression and underexpression under different conditions in living cells *in vitro* and *in vivo*. Thus, while these methods, too, are within the level of skill in the art, Applicant has presented no evidence that any of these validation techniques have, in fact, been carried out with regard to the instantly claimed sequences. As a result, one of skill would be left to de novo screening testing to identify such function, with no assurance that any practical or beneficial function would ever be identified.

Even more, Applicant seeks to claim not only the specified sequence, 7,002,375, but RNA equivalents, complements, and all sequences 80% identical to SEQ ID NO:10,068,310 and equivalents thereto. No evidence is remotely evident suggesting a substantial utility for all these sequences. For example, there is no evidence to suggest a sequence of 16-120 nts in length, 80% identical to SEQ ID NO:10,068,310 could be used to inhibit ACTN4 or produce any immediately available effect of real world value. The claims are extremely broad, encompassing an enormous number of different sequences that could produce any number of different biological effects.

While the asserted utility, stated in the Remarks filed 7/2/07, may be credible and specific, it is not substantial. The specification does not establish a nexus between any particular disease state, bacterial process, or host cell process, and an altered level or form of the claimed SEQ ID NO:7,002,375 that would enable one of skill to use the sequence to achieve a beneficial effect.

While the oligonucleotides of the present invention may be useful for research purposes, in order to further understand the connection between the novel oligonucleotides of the present invention and disease, for disease diagnosis and prevention purposes, and for monitoring disease

progress, these utilities are not specific, since the same can be done with any antisense polynucleotide. And because the specification does not disclose any specific function for the large number of nucleic acids now claimed which may be derived from SEQ ID NO:10,068,310, aside from indicating that it may be expressed in certain cells or present in certain genomes, it is unclear how or why one of skill in the art would use the information obtained by measuring or expressing sequences identical to or RNA equivalents of SEQ ID NO:10,068,310 for any particular purpose aside from general research. Further, since Applicant does not identify whether abnormal SEQ ID NO:10,068,310 expression is causally related to any disease or condition, or whether abnormal SEQ ID NO:10,068,310 function (e.g., a polymorphism) predisposes anyone to any disease or condition—the only recognizable utility of diagnostic probes is as tools for scientific research—and with no indication that anything useful will be discovered. Therefore, the asserted utility is not substantial since the application provides no teaching regarding how to use the probes or expression data for any practical purpose beyond the art-recognized methods of gene expression analysis.

Accordingly, the instantly claimed nucleic acids are simply research intermediates that may be used to conduct further experimentation. The nucleic acids would provide no immediate, real-world information about the overall structure or function of the underlying gene, nor is there any guidance or evidence that the instant nucleic acids, much less the recited RNA equivalents thereof, have any specific biological function. No evidence or information is found either in the specification or the prior art linking SEQ ID NO:10,068,310 or any of its subsequences with the modulation of any gene or inhibition of any condition.

In fact, no evidence is found suggesting or stating that SEQ ID NO:7,002,375 has been made, isolated, cloned, detected, expressed, or even analyzed in a living cell *in vitro* or *in vivo.* In summary, no biological or biochemical function has been assigned to SEQ ID NO: 7,002,375 or 10,068,310, apart from the general assertions that it, like the thousands of other sequences described in the sequence listing, may correspond to an miRNA precursor and have some direct or indirect relation to gene expression and disease.

Thus, the proposed utilities of the instantly claimed nucleic acids as a therapeutic target or agent, or material resource for preparing diagnostic probes, inhibitory agents, vectors, and host cells, are simply starting points for further research and investigation into potential practical uses of the claimed polynucleotides.

> Brenner v. Manson, 148 U.S.P.Q. 689 (U.S. 1966)
>
> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.
>
> …a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.

Thus, the specification does not teach a specific, substantial, or credible utility for SEQ ID NO:10,068,310 or 7,002,375, much less any of the RNA equivalents or complements thereof. No target gene has been conclusively identified nor has any evidence been presented linking the claimed nucleic acids with any target gene, disease, or condition, biological function or disorder. A substantial nexus has not been established.

***

Claims 25, 27, 28, 30, and 31 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25, 27, 28, and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Random Primer 24, sold by New England Biolabs (see page 121 of the 1998/99 New England Biolabs Catalog) (New England Biolabs 1998/99 Catalog, cover page, page 121 and 284).

Given the ambiguity and indefiniteness of Applicant's claims (see rejection under 35 USC §112, second paragraph, above, it is unclear whether the claims encompass or exclude DNA; hence the following prior art rejections are applied over the NEB catalog and Fodor et al.

Furthermore, the the limitation "the complement of any one of (a)-(c)" is interpreted to include both RNA and DNA nucleic acids, since RNA may be complementary to DNA and vice versa. Therefore, the claims embrace both DNA and RNA nucleic acids.

Random Primer 24 contains every possible 24-nucleotide sequence. The following calculations rely on facts provided on page 284 of the catalog, specifically the mass of 1.0 A_{260} unit of single-stranded DNA and the molecular weight of single-stranded DNA per nucleotide (i.e. half the weight of a double-stranded DNA per basepair):

Random 24-mer:

Molecular weight of 24-mer:
24×325 daltons/nucleotide = 7,800 daltons = 7,800 g/mol

Number of possible 24-mers:
$4^{24} = 2.8 \times 10^{14}$ molecules

How many molecules of 24-mer in a vial sold by NEB:
1 A_{260} unit = 33 μg = 3.3×10^{-5} g
3.3×10^{-5} g ÷ 7,800 g/mol = 4.2×10^{-9} mol
$(4.2 \times 10^{-9}$ mol) × $(6.02 \times 10^{23}$ molecules/mol) = 2.5×10^{15} molecules

How many vials needed to sum to 1 of each possible 24-mer:
2.8×10^{14} molecules ÷ 2.5×10^{15} molecules = 0.11 vial

Put another way, every vial of Random Primer 24 sold by New England Biolabs would be expected to contain 9 copies of every possible 24-nucleotide sequence. Therefore, Random Primer 24 would contain every possible gene fragment imaginable that is 24 nucleotides in length.

The Examiner notes the claims are drawn to an "Isolated nucleic acid." However, no clear or limiting definition of the term "isolated" is readily found in the specification that would clearly preclude isolated mixtures of oligonucleotides of the type sold and disclosed by NEB. Given the voluminous nature of the instant application, if Applicant is aware of a definition of the term which would preclude compositions of the type referred to in the instant rejection, Applicant is invited to point to such disclosure in replying to the instant rejection.

Accordingly, the Random Primer 24 sold by New England Biolabs anticipates the instant claims.

***

Claims 25, 27, 28, and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Fodor et al. (US Patent 6,582,908, published as US 2001/0053519 A1 on Dec. 20, 2001).

Fodor et al. taught nucleic acid arrays comprising all possible 20-mers (see claims 4, 7, and 10; and Example 2, beginning at column 22).

Methods for designing and synthesizing "n-mer" arrays to which are attached all possible nucleic acid sequence of a given length, including such calculations as are necessary to design and synthesize all possible oligonucleotides of a given length are taught at columns 17 and 18, for example. For instance, it is said that a 25-mer array would comprise 4^{25} different oligonucleotide sequences.

At column 22, it is taught that at a feature size of 10 μm^2 square micrometers, all possible 10 mers could fit on a single substrate the size of a dime. At a size of 1 μm^2, all possible 20 mers would fit on 100 10 μm^2 substrates. "Thus the present technology provides for making a single substrate of that size having all one million, seven million or more oligonucleotides, depending on the feature size and the size of the substrate. When the number of desired oligonucleotides is so large that a single substrate is impractical, multiple substrates may be used."

Each of the oligonucleotides present on the array are considered to be isolated to the extent they are immobilized in their own particular space on the array.

Accordingly, Fodor et al. taught arrays comprising all possible 20-mers. As such, Fodor et al. taught 20-nucleotide DNA equivalents of the instantly claimed nucleic acids Therefore, Fodor et al. anticipates the instant claims.

***

Claims 25 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Lichter et al. (US Patent 6,432,639).

Lichter et al. disclose a 17-nucleotide DNA, PCR primer, that is at least 80% identical to a complement of SEQ ID NO:10,068,310, as claimed in claim 25 (d). See SEQ ID NO:27 in Table 1, column 14, therein. See also alignment below, also available in SCORE.

Therefore, Lichter et al. anticipates the instant claims.

```
RESULT 7
US-09-144-367-27/c
; Sequence 27, Application US/09144367
; Patent No. 6432639
; GENERAL INFORMATION:
;  APPLICANT: Lichter, Jay
;  APPLICANT:  Guido, Marco
;  TITLE OF INVENTION: GENOTYPING OF HUMAN CYP3A4
;  FILE REFERENCE: SEQ-12P
;  CURRENT APPLICATION NUMBER: US/09/144,367
;  CURRENT FILING DATE:  1998-08-31
;  PRIOR APPLICATION NUMBER: 60/058,612
;  PRIOR FILING DATE: 1997-09-10
;  NUMBER OF SEQ ID NOS: 58
;  SOFTWARE: FastSEQ for Windows Version 3.0
; SEQ ID NO 27
;   LENGTH: 16
;   TYPE: DNA
;   ORGANISM: H. sapiens
US-09-144-367-27

  Query Match              2.7%;  Score 13.4;  DB 3;  Length 16;
  Score over Length       83.8%;
  Best Local Similarity   80.0%;  Pred. No. 1.2e+06;
  Matches   12;  Conservative    2;  Mismatches    1;  Indels    0;  Gaps    0;

Qy        369 ACCACUUCCCAGUAG 383
              |||||::|||||  ||
Db         15 ACCACTTCCCAGGAG 1
```

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Claims 25, 28, and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Stoffel et al. (US 2005/0227934 A1).

Stoffel et al. disclose a ~67-nucleotide pancreatic microRNA hairpin precursor sequence (SEQ ID NO:25) that is 100% identical to residues 11-77 of instant SEQ ID NO:10,068,310. See also alignment below, also available in SCORE. Also disclosed therein are vectors for expressing said precursor miRNAs. See paragraph 39, for example.

Therefore, Stoffel et al. anticipate the instant claims.

```
RESULT 2
AED45485
ID   AED45485 standard; RNA; 67 BP.
XX
AC   AED45485;
XX
DT   15-DEC-2005  (first entry)
XX
DE   Human pancreatic islet microRNA, miR-379 hairpin precursor sequence.
XX
KW   microRNA; miRNA; gene regulation; diabetes; antidiabetic;
KW   endocrine disease; gastrointestinal disease; metabolic disorder; ss.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   misc_feature    6. .24
FT                   /*tag=  a
FT                   /note= "Mature human pancreatic islet miRNA, miR-379"
XX
PN   US2005227934-A1.
XX
PD   13-OCT-2005.
XX
PF   13-APR-2004; 2004US-00824633.
XX
PR   13-APR-2004; 2004US-00824633.
XX
PA   (STOF/) STOFFEL M.
PA   (POYM/) POY M N.
PA   (TUSC/) TUSCHL T H.
XX
PI   Stoffel M,  Poy MN,  Tuschl TH;
XX
DR   WPI; 2005-689467/71.
XX
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PT   New isolated DNA or RNA molecule comprising at least ten contiguous bases
PT   having a sequence in a pancreatic islet microRNA, useful for treating
PT   diabetes.
XX
PS   Claim 2; SEQ ID NO 25; 37pp; English.
XX
CC   The present invention is directed to the discovery of novel pancreatic
CC   islet microRNAs (miRNAs) and anti-pancreatic islet miRNAs that are
CC   complementary to the pancreatic islet miRNAs. microRNAs are typically
CC   small RNA molecules of generally about nineteen to twenty-five
CC   nucleotides in length. They are derived from genomic loci and are
CC   produced from miRNA genes. Mature miRNAs are processed from precursor
CC   transcripts that form local hairpin structures. miRNAs play a role in
CC   gene regulation. The invention further relates to a method of treating
CC   diabetes in a mammal using an anti-pancreatic islet miRNA molecule. The
CC   present sequence is a human pancreatic islet miRNA hairpin precursor
CC   sequence.
XX
SQ   Sequence 67 BP; 19 A; 12 C; 16 G; 0 T; 20 U; 0 Other;

  Query Match             13.4%;  Score 67;  DB 14;  Length 67;
  Score over Length       100.0%;
  Best Local Similarity   100.0%;  Pred. No. 3.7e-12;
  Matches   67;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          11 AGAGAUGGUAGACUAUGGAACGUAGGCGUUAUGAUUUCUGACCUAUGUAACAUGGUCCAC 70
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db           1 AGAGAUGGUAGACUAUGGAACGUAGGCGUUAUGAUUUCUGACCUAUGUAACAUGGUCCAC 60

Qy          71 UAACUCU 77
               |||||||
Db          61 UAACUCU 67
```

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis V. Wollenberger whose telephone number is 571-272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Sean McGarry/
Primary examiner
AU 1635